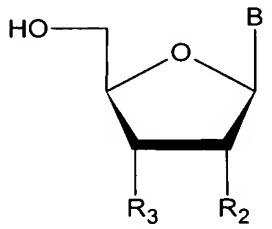
Amendments to the Claims

This listing of claims will replace all prior versions, and listings of claims in the application.

1. (previously presented) A method for preparing an oligonucleotide comprising the steps of

a) providing a 3'-protected compound having the formula:



wherein

B is a heterocyclic base

R_2 is H, a protected 2'-hydroxyl group, F, a protected amino group, an O-alkyl group, an O-substituted alkyl, a substituted alkylamino or a C4′- O2′methylen linkage

R_3 is OR'_3, NHR''_3, $NR''_3R'''_3$, a 3'-protected nucleotide or a 3'-protected oligonucleotide,

R'_3 is a hydroxyl protecting group,

R''_3, R'''_3 are independently an amine protecting group,

b) reacting said compound with a nucleotide derivative having a 5'-proctection group in the presence of a solid supported activator to give an elongated oligonucleotide with a P(III)-internucleotide bond

c) optionally processing the elongated oligonucleotide with a P(III)-internucleotide bond by either or both of steps c1) and c2) in any sequence

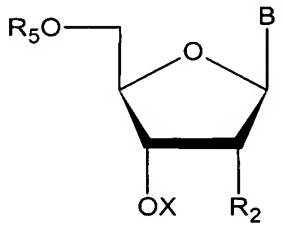
c1) capping preferably by reacting with a solid supported capping agent

c2) oxidizing preferably by reacting the oligonucleotide with a solid supported oxidizing reagent

d) removing the 5'-protection group by treatment with a solid supported agent or removing the 5′-protection group with a removal agent followed by addition of a solid supported scavenger.

e) repeating steps a) to d) at least once.

2. (previously presented) The method of claim 1, wherein the nucleotide derivative having a 5'-proctection group of step b) has the following formula:



wherein

X is a P(III)-function

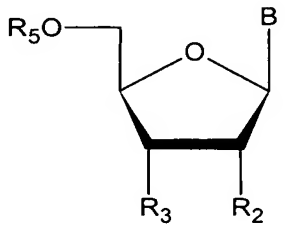
B is a heterocyclic base

R_2 is H, a protected 2'-hydroxyl group, F, a protected amino group, an O-alkyl group, an O-substituted alkyl, a substituted alkylamino or a C4′- O2′methylen linkage

R_5 is a hydroxyl protecting group, a 5'-protected nucleotide or a 5'-protected oligonucleotide.

3. (previously presented) A method for preparing an oligonucleotide comprising the steps of

a) providing a 5'-protected compound having the formula:



wherein

B is a heterocyclic base

R_2 is H, a protected 2'-hydroxyl group, F, a protected amino group, an O-alkyl group, an O-substituted alkyl, a substituted alkylamino or a C4′- O2′methylen linkage

R_3 is OH, NH_2

R_5 is a hydroxyl protecting group, a 5'-protected nucleotide or a 5'-protected oligonucleotide

b) reacting said compound with a nucleotide derivative having a 3'-proctection group in the presence of a solid supported activator to give an elongated oligonucleotide with a P(III)-internucleotide bond

c) optionally processing the elongated oligonucleotide with a P(III)-internucleotide bond by either or both of steps c1) and c2) in any sequence

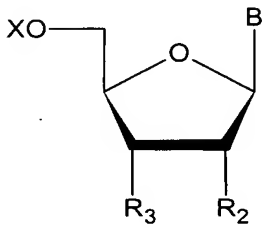
c1) capping, preferably by reacting with a solid supported capping agent

c2) oxidizing, preferably by reacting the oligonucleotide with a solid supported oxidizing reagent

d) removing the 3'-protection group by treatment with a solid supported agent or removing the 3′-protection group with a removal agent followed by addition of a solid supported scavenger.

e) repeating steps a) to d) at least once.

4. (previously presented) The method of claim 3, wherein the nucleotide derivative having a 3'-proctection group has the following formula:



wherein

X is a P(III)-function

B is a heterocyclic base

R_2 is H, a protected 2'-hydroxyl group, F, a protected amino group, an O-alkyl group, an O-substituted alkyl, a substituted alkylamino or a C4′- O2′methylen linkage

R_3 = OR′$_3$, NHR"$_3$, NR"$_3$R'"$_3$, a 3'-protected nucleotide or a 3'-protected oligonucleotide,

R′$_3$ is a hydroxyl protecting group,

R"$_3$, R'"$_3$ are independently an amine protecting group,

R′$_3$ is a hydroxyl protecting group, a 3'-protected nucleotide or a 3'-protected oligonucleotide.

5. (currently amended) The method of ~~any one of claims 1 to 4~~ claim 1, wherein the nucleotide derivative of step b) is a phosphoramidite or a H-phosphonate.

6. (currently amended) The method of ~~any one of steps 1 to 5~~ claim 1, wherein the solid supported activator of step b) is selected from the group consisting of a solid support bearing a pyridinium salt, a cation exchange solid support with an optionally substituted pyridinium, a cation exchange solid support with an optionally substituted imidazolium salt, a solid support bearing an optionally substituted azole (imidazol, triazole, tetrazole), a salt of a weak base anion exchange resin with a strong acid, a weak cation exchange resin (carboxylic) in its protonated form, a solid support bearing an optionally substituted phenol, a solid support bearing a carboxylic acid chloride/bromide, a sulfonic acid chloride/bromide, a chloroformate, a bromoformate, a chlorosulfite, a bromosulfite, a phosphorochloridate, a phosphorbromidate and a solid support bound carbodiimide.

7. (currently amended) The method of ~~any one of claims 1 to 6~~ claim 1, wherein the solid supported oxidizing reagent is selected from the group consisting of solid supported periodates, permanganates, osmium tetroxides, dichromates, hydroperoxides, substituted alkylamine oxides, percarboxylic acid and persulfonic acid.

8. (currently amended) The method of ~~any one of claims 1 to 7~~ claim 1, wherein the oxidizing is a sulfurization.

9. (previously presented) The method of claim 8, wherein the solid supported oxidizing reagent is selected from the group consisting of a solid supported tetrathionate, a solid supported alkyl or aryl sulfonyl disulfide, a solid supported optionally substituted dibenzoyl tetrasulfide, a solid supported bis(akyloxythio-carbonyl)tetrasulfide, a solid supported optionally substituted phenylacetyl disulfide, a solid supported N-[(alkyl or aryl)sulfanyl] alkyl or aryl substituted succinimide and a solid supported (2-pyridinyldithio) alkyl or aryl.

10. (currently amended) The method of ~~any one of claims 1 to 9~~ claim 1, wherein the solid supported capping agent is a solid supported activated acid, preferably a carboxylic acid chloride, carboxylic acid bromide, azolide, substituted azolide, anhydride or chloroformate or phosphorochloridate, or a solid supported phosphoramidite, or a solid supported H-phosphonate monoester.

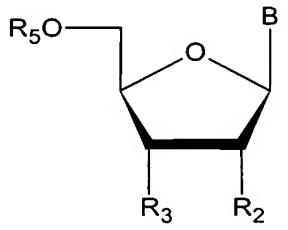
11. (currently amended) The method of ~~any one of claims 1 to 10~~ claim 1, wherein the 5′-protection is a dimethoxytrityl group (DMTr) or a monomethoxytrityl group (MMTr) and the solid supported agent of step d) is an cationic ion exchanger resin in the H^+ form or solid supported ceric ammonium nitrate.

12. (currently amended) The method of ~~any one of claims 1 to 11~~ claim 1, wherein the 3′-protection is a silyl group and the solid supported agent of step d) is an anionic ion exchanger resin in the F-form or the 3′-proctection is levulinic acid and the solid supported agent of step d) is a solid supported hydrazine or a solid supported hydrazinium.

13. (cancelled)

14. (previously presented) A method for preparing an oligonucleotide comprising the steps of

a) providing a compound having the formula:



wherein

B is a heterocyclic base

R_2 is H, a protected 2'-hydroxyl group, F, a protected amino group, an O-alkyl group, an O-substituted alkyl, a substituted alkylamino or a C4′- O2′methylen linkage and

R_3 is OR'_3, NHR''_3, $NR''_3R'''_3$,

a protected nucleotide or a protected oligonucleotide and R_5 is a P(III) function

R'_3 is a hydroxyl protecting group,

R''_3, R'''_3 are independently an amine protecting group,

or

R_5 is a hydroxyl protecting group, a protected nucleotide or a protected oligonucleotide and R_3 is a P(III) function

b) reacting said compound with a nucleotide derivative having a 3' or 5'-free OH-group in the presence of a solid supported activator to give an elongated oligonucleotide with a P(III)-internucleotide bond

c) optionally processing the elongated oligonucleotide with a P(III)-internucleotide bond by either or both of steps c1) and c2) in any sequence

c1) capping by reacting with a solid supported capping agent

c2) oxidizing by reacting the oligonucleotide with a solid supported oxidizing reagent

d) removing the 3' or 5'-protection group by treatment with a solid supported agent or removing the 5'-protection group with a removal agent followed by addition of a solid supported scavenger.

e) repeating steps a) to d) at least once.

15. (new) The method of claim 3, wherein the nucleotide derivative of step b) is a phosphoramidite or a H-phosphonate.

16. (new) The method of claim 3, wherein the solid supported activator of step b) is selected from the group consisting of a solid support bearing a pyridinium salt, a cation exchange solid support with an optionally substituted pyridinium, a cation exchange solid support with an optionally substituted imidazolium salt, a solid support bearing an optionally substituted azole (imidazol, triazole, tetrazole), a salt of a weak base anion exchange resin with a strong acid, a weak cation exchange resin (carboxylic) in its protonated form, a solid support bearing an optionally substituted phenol, a solid support bearing a carboxylic acid chloride/bromide, a sulfonic acid chloride/bromide, a

chloroformate, a bromoformate, a chlorosulfite, a bromosulfite, a phosphorochloridate, a phosphorbromidate and a solid support bound carbodiimide.

17. (new) The method of claim 3, wherein the solid supported oxidizing reagent is selected from the group consisting of solid supported periodates, permanganates, osmium tetroxides, dichromates, hydroperoxides, substituted alkylamine oxides, percarboxylic acid and persulfonic acid.

18. (new) The method of claim 3, wherein the oxidizing is a sulfurization.

19. (new) The method of claim 18, wherein the solid supported oxidizing reagent is selected from the group consisting of a solid supported tetrathionate, a solid supported alkyl or aryl sulfonyl disulfide, a solid supported optionally substituted dibenzoyl tetrasulfide, a solid supported bis(akyloxythio-carbonyl)tetrasulfide, a solid supported optionally substituted phenylacetyl disulfide, a solid supported N-[(alkyl or aryl)sulfanyl] alkyl or aryl substituted succinimide and a solid supported (2-pyridinyldithio) alkyl or aryl.

20. (new) The method of claim 3, wherein the solid supported capping agent is a solid supported activated acid, preferably a carboxylic acid chloride, carboxylic acid bromide, azolide, substituted azolide, anhydride or chloroformate or phosphorochloridate, or a solid supported phosphoramidite, or a solid supported H-phosphonate monoester.

21. (new) The method of claim 3, wherein the 5′-protection is a dimethoxytrityl group (DMTr) or a monomethoxytrityl group (MMTr) and the solid supported agent of step d) is an cationic ion exchanger resin in the H^+ form or solid supported ceric ammonium nitrate.

22. (new) The method of claim 3, wherein the 3′-protection is a silyl group and the solid supported agent of step d) is an anionic ion exchanger resin in the F-form or the 3′-proctection is levulinic acid and the solid supported agent of step d) is a solid supported hydrazine or a solid supported hydrazinium.

23. (new) A method for sulfurization of an oligonucleotide with a P(III) internucleotide bond comprising the step of

oxidizing with a solid supported sulfurization agent consisting of a solid supported amine and a tetrathionate having the formula S_4O_6 or a cyanoethylthiosulfate ($NC\text{-}CH_2\text{-}CH_2\text{-}S\text{-}SO_3^-$).